



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,603	02/13/2006	Hildegund C. J. Ertl	WSTR-0020C	1578
26259 7590 05/31/2007 LICATA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053				
			EXAMINER SINGH, ANOOP KUMAR	
			ART UNIT 1632	PAPER NUMBER
			MAIL DATE 05/31/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/559,603

Applicant(s)

ERTL, HILDEGUND C. J.

Examiner

Anoop Singh

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>2/13/2006</u> | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Claims 1-22 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim embraces orally administering any adenoviral vector encoding any transgene product to induce an immune response. Subsequent claims limit the scope of transgene product to include any protein from a cancer cell or aberrant protein or any antigenic epitope. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-cath Inc. v. Mahurkar*, 19USPQ2d at 1 117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

In analyzing whether the written description requirement is met for the genus claim, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics, specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, orally administering any adenoviral vector encoding any transgene

product that include know or unknown cancer protein or aberrant protein that induces immune response, encompassed within the genus of adenoviral vector encoding any transgene product.

The specification describes the AdHu5rab.gp recombinant, an E1 deletion Ad recombinant of the human serotype 5 expressing the glycoprotein of the ERA strain of rabies virus (see example 1, page 38 of the specification). In addition, specification has described mice are immunized once or twice with various doses of the AdHu5 or AdC68 constructs given orally or intramuscularly (i.m.) (see page 39-40, example 2). It is noted that specification contemplated transgene product may include any known or known cancer cell protein, any sequence that has been mutated (see specification page 29, line 25-26), or genus of transgene derived from bacterium, virus or mycoplasma (see page 28-30). However, specification fails to provide any particular structure to function/activity relationship in this single disclosed species for use in the invention for genus of adenoviral vector encoding transgene products capable of inducing immune response except those exemplified in the instant application. Prior to instant invention Sharpe et al (Virology. 2002, 293, 210-216, IDS) disclose oral immunization with recombinant adenoviruses have largely focused on replication competent constructs and oral immunization of mice with E3- recombinant adenovirus expressing rotavirus VP7 induced serum antibody showed responses levels than those seen following intraperitoneal, intravenous, or intranasal delivery. This is further supported by another human clinical trial, involving oral administration of adenoviral vector that failed to induce transgene-specific immunity. Sharpe et al conclude that "Overall, replication-competent adenoviruses appear to require a degree of active replication in the vaccinated host in order to stimulate effective transgene-specific immune response (see page 312 col. 2, last para, bridging to 314, col. 1, para. 1). There is no evidence on record that pre exposure or orally administering any adenoviral vector encoding a transgene product would induce immune response against the product. Further, claims embrace any transgene product including any known or unknown protein made by any cancer cell. Carbone et al. (Seminars in Cancer Biology, 2004, 14: 399-405) teach "the prognosis of metastatic carcinoma ... has not significantly changed during the past 40

years... because advanced solid tumors are genetically heterogeneous both among cases and within the same patient. They are also genetically instable. Prior art also teaches that a minor structural difference in protein could result in substantially different activities. The specification has not disclosed the structure of genus of known and unknown protein made by cancer cell nor does identified any common structure or attribute that is present in genus of transgene product and would be functional as contemplated by the specification.

The claimed invention as a whole is not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). The specification fails to describe what structure or sequence of adenoviral vector or transgene product other than exemplified in the specification fall into the genus that has contemplated biological activity of binding to a vector and transgene product. The skilled artisan cannot envision the detailed chemical structure of the all the molecule or sequences showing contemplated biological activity, and therefore conception are not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the composition.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In view of the above considerations, one of skill in the art would not recognize that applicant was not in possession of the necessary common features or attributes possessed by member of the genus of adenoviral vector

Art Unit: 1632

or transgene products, other than the ones exemplified in the specification. Therefore, Applicant was not in possession of the genus of adenoviral vector encoding any transgene product showing contemplated biological activity as encompassed by the claims. *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Lubeck et al (Proc Natl Acad Sci U S A. 1989; 86(17): 6763-7).

Lubeck et al teach a method for inducing an immune response to a transgene product in chimpanzees following oral administration of live human adenoviruses type 7 (Ad7) and type 4 (Ad4) virus. Lubeck et al disclose oral immunization with Ad7- and Ad4-vectored vaccines containing the hepatitis B surface antigen (HBsAg) gene showing significant induction of antibody responses to HBsAg (anti-HBs) in two chimpanzees (abstract and figure 2). In addition, Lubeck et al disclose screening chimpanzees for type specific neutralizing antibody and report 77% of the animals had significant anti-Ad4 antibody titers (see page 6764, col. 2, result section, para. 1). In addition, Lubeck et al also disclose that seroprevalence study of chimpanzees indicated substantial preexisting immunity to Ad4 but not to Ad7, thus any primary vaccination to such chimpanzees to recombinant Ad7 or Ad4 would meet the limitation of claims 3 and 5 (see page 6767, col. 1, para4 and table 1). It is noted that chimpanzees with low

neutralizing antibody were selected to receive primary oral immunizations with Ad7 or Wy-Ad7HZ6-1 followed by 11 weeks later oral booster vaccinations with Wy-Ad4HHxHS (see page 6764, col. 2, last para and Table 2).

Accordingly, Lubeck et al anticipates, claim 1-6.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (WO 99/08706, dated 2/25/1999).

Johnson et al teach a method for inducing an immune response to a transgene product by administering adenoviral vectors for antigen producing genes in commercial pigs susceptible to decimation by disease. (see page 1, lines 1-10 and page 2, lines 21-25). It is noted that Johnson et al contemplate that heterologous nucleotide sequence may encode for and/or express, an antigenic polypeptide and an immuno-potentiator molecule (see page 2, lines 27-29). Johnson et al disclose porcine adenoviral vector may express antigenic determinant of porcine parvo, rota or corona virus and may encode for adjuvant such as IL-4, GMCSF or IL-3 (see page 6, line 15-20). Johnson et al disclose a method of vaccination of pigs against disease comprises administering to pigs a first recombinant porcine adenovirus vector stably incorporating at least one nucleotide sequence encoding an antigenic determinant and also administering to the pig a second porcine adenovirus vector including at least one heterologous nucleotide sequence which differs from said at least one heterologous nucleotide sequence incorporated in said first recombinant porcine adenovirus vector. Johnson et al also disclose that the second porcine adenovirus vector comprises at least one heterologous nucleotide sequence encoding an immuno-potentiating molecule (see claims 39-42, pages 31-32). It is noted that Johnson et al discloses that heterologous antigen and immuno-modulatory molecule such as a cytokine may be expressed in the same recombinant and delivered as a single vaccine. PAV vector based vaccines may be administered orally or intra nasally (see page 11, line 11 and claim 37, page 31) consecutively of each other to administer either booster vaccines or new vaccines at some stage subsequent to initial PAV vaccination (See page 10, lines 2-12).

Accordingly, Johnson et al anticipate claims 1-4, 6-8

Claims 1-2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Fooks et al (J Gen Virol. 1998; 79 (Pt 5): 1027-31).

Fooks teaches a method to induce low levels of MV specific IgG and protective response in mice that are immunized by orally administering an adenoviral vector RAd88 or RAd95 encoding MV H or F protein in two doses containing 10^8 pfu one week apart (see page 1028, col. 2, para. 1, Figure 2b and page 1039, col. 1, lines 2-3). It is noted that that first and second adenoviral vector encodes same transgene product which is genes encoding for measles virus (MV) haemagglutinin (H) and fusion (F) proteins under the control of the human cytomegalo virus immediate early promoter in the replication-deficient adenovirus vector (abstract).

Accordingly, Fooks et al anticipate claims 1-2 and 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lubeck et al (Proc Natl Acad Sci U S A. 1989; 86(17): 6763-7) or Natuk et al (AIDS research an Human retrovirus, 1993, 9, 5 395-404) and Velin et al (Pathobiology, 1998, 66, 170-175, IDS).

Lubeck et al teach a method for inducing an immune response to a transgene product in chimpanzees following oral administration of live human adenoviruses type 7 (Ad7) and type 4 (Ad4) virus. Lubeck et al disclose oral immunization with Ad7- and

Ad4-vectored vaccines containing the hepatitis B surface antigen (HBsAg) gene showing significant induction of antibody responses to HBsAg (anti-HBs) in two chimpanzees (abstract and figure 2). In addition, Lubeck et al disclose screening chimpanzees for type specific neutralizing antibody and report 77% of the animals had significant anti-Ad4 antibody titers (see page 6764, col. 2, result section, para. 1). In addition, Lubeck et al also disclose that seroprevalence study of chimpanzees indicated substantial preexisting immunity to Ad4 but not to Ad7, thus any primary vaccination to such chimpanzees to recombinant Ad7 or Ad4 would meet the limitation of claims 3 and 5 (see page 6767, col. 1, para 4 and table 1). It is noted that chimpanzees with low neutralizing antibody were selected to receive primary oral immunizations with Ad7 or Wy-Ad7HZ6-1 followed by 11 weeks later oral booster vaccinations with Wy-Ad4HHxHS (see page 6764, col. 2, last para and Table 2). However, Lubeck differed from claimed invention by not disclosing that adenoviral vector further encodes an adjuvant.

Natuk et al teach cell mediated and humoral immune response to recombinant HIV antigen following orally immunizing chimpanzees that were sero-negative for Ad4, 5 or 7 but pre exposed to other strains of wild type adenovirus by administering Ad-HIV recombinant viral vector for three successive days (see page 396, col. 2, para. 3). It is noted that two different group of chimpanzees also received booster immunization of adenoviral vector expressing env and gag gene meeting the claim limitation. However, Natuk differed from claimed invention by not disclosing that adenoviral vector further encodes an adjuvant.

However, at the time the claimed invention was made inclusion of adjuvant to induce immune response by administering adenoviral vector was within the routine skill level of the ordinary artisan. It was also well known at the time the invention was made that oral delivery of mucosal adjuvant in association with antigen enhanced mucosal and systemic immune response against them. For instance, Velin et al teach antigen must be delivered to a mucosal antigen-sampling site, such as the Peyer's patches of the small intestine in order to elicit a mucosal immune response. Velin taught strategies to avoid tolerance after oral administration of vaccine by using mucosal adjuvants such as cholera toxin or heat-labile enterotoxin of *Escherichia coli* that enhance immune

Art Unit: 1632

responses to the antigen of interest. In addition, Velin et al also disclose attenuated *Salmonella typhimurium* that triggers mucosal and systemic immune responses after vaccination of BALB/c mice via the oral routes with attenuated *Salmonella* expressing a foreign antigen such as the nucleocapsid protein of hepatitis B virus. This has been shown to induce a strong mucosal and systemic immune response against themselves and the carried antigen. Velin teaches oral or nasal vaccination with recombinant *Salmonella* induces strong IgA responses in saliva; vaginal secretions, feces and intestinal secretions directed the carrier and the carried antigen (see page 173, col1, last para and col. 2, para. 1 and 2). Velin et al also disclose the adenovirus vector have been extensively used for inducing systemic and mucosal immune response, however emphasize that these vectors should be further characterized in addition to mechanism of action of mucosal adjuvant (see page 174, col. 1, para. 2 and col. 2, para. 2, conclusion).

Accordingly, in view of the teachings of Lubeck/ Natuk and Velin, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the method of inducing immune response disclosed by Lubeck/ Natuk to include adjuvant as disclosed by Velin. Lubeck/ Natuk had already taught a method to induce immune response by orally administering a subject effective amount of combination of adenoviral vector encoding a transgene product (*supra*). It is noted that at the time of filing of this application use of adjuvant to boost mucosal immune response was also known in the art as taught by Velin and discussed above. One of ordinary skill in the art would be motivated to use an adenoviral vector encoding an adjuvant in order to elicit a mucosal immune response and also avoid tolerance after oral administration of vaccine as taught by Velin.

One who would practiced the invention would have had reasonable expectation of success because Lubeck/ Natuk had already taught that methods to induce immune response by orally administering a combination of adenoviral vector encoding a transgene product. Velin used adjuvant to overcome the problem of tolerance after oral administration of vaccine and in order to induce mucosal immune. Thus, it would have only required routine experimentation to modify the method of Lubeck/ Natuk to further

include administration of adenoviral encoding an adjuvant to optimize the induction of mucosal immune response.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lubeck et al (Proc Natl Acad Sci U S A. 1989; 86(17): 6763-7)/ Natuk et al (AIDS research an Human retrovirus, 1993, 9, 5 395-404), Velin et al (Pathobiology, 1998, 66, 170-175, IDS) and Mutiwiri et al (Vaccine, 2001, 1284-1293, IDS).

The combined teachings of Lubeck et al/ Natuk et al and Vile have been discussed above and relied in same manner here. However, none of the reference explicitly teaches a method for inducing an immune response in an infant by orally administering an adenoviral vector encoding a transgene so that immune response to transgene is induced.

Mutiwiri et al disclose enteric immunization of newborn lambs. It is noted that samples from blood and colostrums of eight pregnant ewes that are divided into two equal groups show immunization (+passive Ab) and that naive ewes had low levels of gD-specific antibody (-passive Ab) (see page 1285, col. 2, para. 2). Mutiwiri teach a method to determine if enteric immunization of newborn lambs could prime mucosal immune responses. It is noted that one group of lambs are immunized by injecting HAd5-gD/E3 vector into intestinal 'loops,' containing jejunal PP, while second group is immunized with s.c. injection of HAd5-gD/E3 vector (see page 1285, col.2, para. 3). The results show recombinant adenovirus vaccine vector into an intestinal 'loop' containing a jejunal PP of newborn lambs induced both humoral and cell-mediated mucosal immune responses (see Figure 3, 4 and 6 and page 1289, col. 2, para. 3-4, page 1292, col. 1, para 2). Mutiwiri concludes the oral vaccines may be an effective approach for the induction of active immunity in the numerous species that have prenatal development of GALT. Furthermore, he also contemplates to combine the passive transfer of maternal antibody with the induction of active immunity to provide optimal disease protection in

Art Unit: 1632

the newborn (see page 1292, col. 1, last para.). Although, the disclosure by Mutiwiri indirectly taught a method to induce immune response by enteric immunization of newborn lamb, but Mutiwiri differed from claimed invention by not explicitly teaching an adenoviral vector that is administered orally and encodes an adjuvant.

Accordingly, in view of the teachings of Mutiwiri et al, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the method of inducing immune response of Mutiwiri in infants by orally administering an adenoviral vector that encodes for a transgene product that may also further encode an adjuvant. One of ordinary skill in the art would be motivated to administer oral vaccine in order to induce immune response as shown by Lubeck et al/ Natuk et al. It is noted that at the time of filing of this application use of adjuvant and different route to prime-boost humoral or mucosal immune response was also known in the art as taught by Velin (*supra*). One of ordinary skill in the art would be motivated to modify the method to orally administer adenoviral vector encoding transgene or an adjuvant particularly since Mutiwiri taught (i) immature immune system and (ii) maternal antibody interference with vaccines contributes to the ineffectiveness of parental administration. Mutiwiri attributes this failure to the presence of passively acquired maternal antibodies (see page 1284, col. 2, para. 1).

One who would practice the invention would have had reasonable expectation of success because Lubeck/ Natuk had already taught method to induce immune response by orally administering a combination of adenoviral vector encoding a transgene product. Velin used adjuvant to overcome the problem of tolerance after oral administration of vaccine and in order to induce mucosal immune. Mutiwiri taught a method to induce immune response by immunization of newborn lamb to induce effective immune response. Thus, it would have only required routine experimentation to modify the method to include administration of adenoviral encoding a transgene product with or without an adjuvant for the induction of humoral and or mucosal immune response in infants.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lubeck et al (Proc Natl Acad Sci U S A. 1989; 86(17): 6763-7)/ Natuk et al (AIDS research an Human retrovirus, 1993, 9, 5 395-404), Velin et al (Pathobiology, 1998, 66, 170-175, IDS) and Yarosh et al (Vaccine. 1996; 14(13): 1257-64, IDS) and Mittal (Vaccine. 2000; 19(2-3):253-63).

The combined teachings of Lubeck et al/ Natuk et al and Velin have been discussed above and relied in same manner here. However, none of the reference explicitly teaches systemically administering the adenoviral vector.

Yarosh et al disclose administering human adenoviral vector expressing rabies glycoprotein to mice and skunks (abstract, col. 1, materials and method), wherein the adenovirus was administered to mice by ip injection and to the skunks by oral vaccination (page 1259, col. 1). It is noted that Yarosh et al also teach both route of administration were able to induce immune response in the host animal (page 1261, table 1, page 1262, table 2). However, Yarosh et al differed from claimed invention by not disclosing administering adenoviral vector by oral and i.p route in same animal.

Mittal taught role of systemic routes of immunization (i.m., s.c. and i.p.) resulted in higher BAd3-specific IgG titers compared to those obtained by mucosal routes of inoculation (oral and i.n.), however, mucosal immunization led to higher titers of BAd3-specific IgA at mucosal sites compared to those obtained by the various systemic routes. Kanellos also disclose the advantage of using immune stimulatory molecules such as cytokine genes, cholera toxin, CpG motifs in modulating immune responses.

Accordingly, in view of the teachings of Lubeck/ Natuk, Velin, Yarosh et al and Mittal, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the method of inducing immune response of Lubeck/ Natuk by using adjuvant so that one of the adenoviral vector may encode for an adjuvant. Furthermore, one of ordinary skill in the art would be motivated to use

Art Unit: 1632

combination of oral and systemic route to administer vaccine in order to induce cell mediated, humoral and mucosal immunity as shown by Mittal. It is noted that at the time of filing of this application use of adjuvant and different route to prime-boost humoral or mucosal immune response was also known in the art as taught by Velin and Mittal (supra). One of ordinary skill in the art would be motivated to use combination of adenoviral vector encoding transgene or an adjuvant by administering them orally or orally and systemically in order to get humoral or robust mucosal immune response as taught by Mittal.

One who would practiced the invention would have had reasonable expectation of success because Lubeck/ Natuk had already taught methods to induce immune response by orally administering a combination of adenoviral vector encoding a transgene product. Velin used adjuvant to overcome the problem of tolerance after oral administration of vaccine and in order to induce mucosal immune. Yarosh et al also teach both i.p and oral route of administration were able to induce immune response in the host animal, while mucosal administration resulting in higher mucosal immune response. Thus, it would have only required routine experimentation to modify the method to further include administration of adenoviral encoding an adjuvant and administer in combination with other adenoviral vector encoding transgene via systemically and or orally to optimize the induction of humoral and or mucosal immune response.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No Claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Vos et la (Journal of General Virology, 2001, 82, 2191-2197, IDS).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anoop Singh, Ph.D.
AU 1632

/Anne-Marie Falk/

Primary Examiner, Art Unit 1632